(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 January 2001 (04.01.2001)

PCT

(10) International Publication Number
WO 01/00612 A2

(51) International Patent Classification[7]: C07D 401/12, A61K 31/437, 31/4465, 31/4545, A61P 11/00, 31/12, C07D 471/04, 401/14 // (C07D 471/04, 235:00, 221:00)

(21) International Application Number: PCT/EP00/05675

(22) International Filing Date: 20 June 2000 (20.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
99202088.3 28 June 1999 (28.06.1999) EP

(71) Applicant *(for all designated States except US)*: JANSSEN PHARMACEUTICA N.V. [BE/BE]; c/o De Corte, Filip - Ext. 3834, Patent Dept., Turnhoutseweg 30, B-2340 Beerse (BE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: JANSSENS, Frans, Eduard [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). MEERSMAN, Kathleen, Petrus, Marie-José [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). SOMMEN, François, Maria [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). ANDRIES, Koenraad, Jozef, Lodewijk, Marcel [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE).

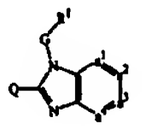
(74) Agent: QUAGHEBEUR, Luc; Janssen Pharmaceutica N.V., Patent Dept. - 3547, Turnhoutseweg 30, B-2340 Beerse (BE).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

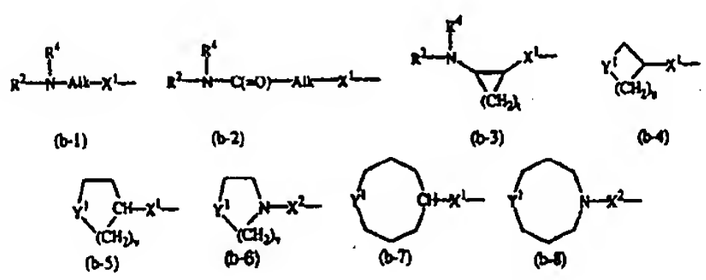
(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European

[Continued on next page]

(54) Title: RESPIRATORY SYNCYTIAL VIRUS REPLICATION INHIBITORS



(I)



(57) Abstract: This invention concerns the compounds of formula (I), prodrugs, <I>N</I>-oxides, addition salts, quaternary amines, metal complexes or stereochemically isomeric forms thereof wherein -a^1=a^2-a^3=a^4- is a radical of formula -CH=CH-CH=CH-, -N=CH-CH=CH-, -CH=N-CH=CH-, -CH=CH-N=CH-, -CH=CH-CH=N- wherein each hydrogen atom may optionally be substituted; Q is a radical of formula (b-1), (b-2), (b-3), (b-4), (b-5), (b-6), (b-7), (b-8), wherein Alk is C_{1-6}alkanediyl; Y^1 is a bivalent radical of formula-NR^2- or -$CH(NR^2R^4)$-; X^1 is NR^4, S, S(=O), $S(=O)_2$, O, CH_2, C(=O), $CH(=CH_2)$, CH(OH), $CH(CH_3)$, $CH(OCH_3)$, $CH(SCH_3)$, $CH(NR^{5a}R^{5b})$, CH_2-NR^4 or NR^4-CH_2; X^2 is a direct bond, CH_2, C(=O), NR^4, C_{1-4}alkyl-NR^4, NR^4-C_{1-4}alkyl; t is 2 to 5; u is 1 to 5; v is 2 or 3; and whereby each hydrogen in Alk and in (b-3), (b-4), (b-5), (b-6), (b-7) and (b-8), may optionally be replaced by R^3; provided that when R^3 is hydroxy or C_{1-6}alkyloxy, then R^3 can not replace a hydrogen atom in the α position relative to a nitrogen atom; G is substituted C_{1-10}alkanediyl wherein the substituent is attached via an oxygen atom; R^1 is an optionally substituted monocyclic heterocycle or aryl; R^2 is hydrogen, formyl, C_{1-6}alkylcarbonyl, Hetcarbonyl, pyrrolidinyl, piperidinyl, homopiperidinyl, C_{3-7}cycloalkyl or C_{1-10}alkyl substituted with $N(R^6)_2$ and optionally with another substituent; R^3 is hydrogen, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy, arylC_{1-6}alkyl or arylC_{1-6}alkyloxy; R^4 is hydrogen, C_{1-6}alkyl or arylC_{1-6}alkyl; R^{5a}, R^{5b}, R^{5c} and R^{5d} are hydrogen or C_{1-6}alkyl; or R^{5a} and R^{5b}, or R^{5c} and R^{5d} taken together form a bivalent radical of formula -$(CH_2)_s$- wherein s is 4 or 5; R^6 is hydrogen, C_{1-4}alkyl, formyl, hydroxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl or C_{1-6}alkyloxycarbonyl; aryl is optionally substituted phenyl; Het is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl; as respiratory syncytial virus replication inhibitors; their preparation, compositions containing them and their use as a medicine.

WO 01/00612 A2

patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— *Without international search report and to be republished upon receipt of that report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.